MEDICAL SCIENCES

PATHOGENETIC ASPECTS, DIAGNOSIS AND PRINCIPLES OF TREATMENT OF NEWBORN HYPOGLYCAEMIA

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Introductions. Glucose is one of the components of the internal environment of the body, the concentration of which in the blood is maintained at a relatively constant level. Conditions associated with an increase or decrease in blood glucose are dangerous to the body. In clinical medicine, very much attention is paid to hyperglycemia, but hypoglycemia is quite common, especially in infants in the neonatal period. Hypoglycemia in infants occurs with a frequency of 1-3 cases per 1000 live births, and in infants with low birth weight it is observed in 14.7%. Decreased blood sugar in a child can be a symptom of severe hereditary metabolic disorders. It is known that the frequency of hereditary diseases with hypoglycemia is

1: 50,000 live births, of which the deficiency of acyl-CoA dehydrogenase with a medium chain (MCAD) – 1: 4900-1: 17000; incidence of hyperinsulinism – 1: 2500.

The most common causes of persistent hypoglycemia in newborns are low gluconeogenesis due to congenital enzyme defects and disorders of hormonal regulation. Congenital metabolic disorders can be manifested by episodes of hypoglycemia during metabolic crises, which can be life-threatening if not diagnosed and treated in time. The first manifestation of a congenital metabolic error can be at any age, and most cases occur during metabolic stress or transition, with various diseases or changes in diet. Therefore, a preliminary diagnosis should be made as soon as possible and treatment of the sick newborn should be started.

Aim. To generalize modern ideas about the pathogenesis, diagnosis and principles of treatment of neonatal hypoglycemia.

Materials and methods. Scientific publications for the last 10 years, methodical recommendations, clinical cases concerning definition of modern views on pathogenetic mechanisms, diagnostics and treatment of persistent hypoglycemia in the neonatal period are investigated.

Results and discussion. Blood glucose is the main energy substrate for the central nervous system; metabolite for the synthesis of other monosaccharides, lipids, proteins, neurotransmitters. Due to glycolysis and oxidative phosphorylation, glucose is the main source of cellular energy (ATP). The brain mainly uses glucose metabolism to produce energy and is particularly sensitive to hypoglycemia. In the fetus, about 50% of the body's total energy needs are provided by glucose, another half - amino acids and lactate. The fetus up to 70% depends on the level of glucose in the mother's blood, because he can not actively form it. After birth, normoglycemia is provided by enteral carbohydrate intake and own endogenous glucose production: hepatic gluconeogenesis, glycogenolysis. Due to the physiological immaturity of carbohydrate homeostasis, half of healthy infants are unable in the first 12 hours after birth to maintain normal fasting plasma glucose levels, and the use of alternative energy sources in the neonatal period is limited. In addition, there are a number of

perinatal factors, such as asphyxia, sepsis, hypothermia, maternal diabetes, prematurity, and others that lead to prolonged hypoglycemia.

Hypoglycemia is defined as a decrease in blood glucose less than 2.6 mmol/L in both full-term and premature infants. For premature infants, levels of 2.0 mmol/L in the first 2-3 hours of life and less than 2.6 mmol/L between 4 and 24 hours of life are indicated. Contradictory opinions concerning the level of normoglycemia are associated with the use of various methods to determine the "safe" level of glucose. The severity of hypoglycemia depends on the gestational and chronological age of the child and other risk factors in addition to low blood glucose. There is no single indicator below which brain damage occurs. The absence of severe symptoms at low glucose levels does not preclude CNS damage.

In newborns, serum glucose levels stabilize approximately 12 hours after birth to 2.6 mmol/L. In a healthy state, glucose homeostasis is the basis of strict regulation by glucose-lowering hormones (insulin) and hormones that mobilize glucose (cortisol, growth hormone, etc.), affecting glycolysis, gluconeogenesis, glycogenolysis, and other metabolic processes, catabolism or transport of carbohydrates, lipids and amino acids. Newborns are at particular risk of hypoglycemia because they use glucose faster than adults and have an immature ability to receive energy from other sources (glycogen, muscle protein, adipose tissue).

Thus, the body maintains a balance between the formation of glucose and its use; at birth, the newborn switches to the independent formation of glucose; in the postnatal period, the maintenance of homeostasis depends on the balance between glucose synthesis by the liver and its consumption by tissues. Premature babies are at risk for the development of hypoglycemia due to lower energy reserves, higher insulin concentrations, underdeveloped mechanisms of gluconeogenesis, reduced concentrations of other metabolic substrates, as well as glucagon. The above changes are even more characteristic of children "immature before gestation."

Depending on the etiology and pathogenesis, neonatal hypoglycemia can be transient and persistent. Causes of transient hypoglycemia: transient hyperinsulinism,

transient glucose deficiency, drug-induced hypoglycemia, etc. All newborns at risk (from mothers with diabetes, premature, with intranatal hypoxia) should be screened for blood glucose immediately after birth. If hypoglycemia or the need for glucose infusions persists for more than a week, congenital metabolic defects or endocrine abnormalities should be considered.

Almost all congenital metabolic disorders that cause hypoglycemia are inherited by autosomal recessive type. Congenital hyperinsulinism – by BP or AR-type; glycerol kinase deficiency is linked to the X chromosome.

Etiopathogenesis of persistent hypoglycemia:

1. Congenital hyperinsulinism: mutations in the genes SUR1, KIR6.2, glucokinase, glutamate dehydrogenase; disorders of fatty acid metabolism; congenital disorders of glycosylation; insulinoma.

2. Deficiency of counterinsular hormones: cortisol, adrenocorticotropic hormone, thyroid-stimulating hormone, somatotropic hormone, glucagon, adrenaline.

3. Disorders of glycogen release/accumulation in the liver: glucose-6-phosphatase deficiency; amylo-1,6-glucosidase deficiency; phosphorylase deficiency; α-1,4-glucosidase deficiency; amylo-1,6-glucosidase deficiency; lack of muscle phosphorylase; hepatic glycogen synthetase deficiency.

4. Disorders of gluconeogenesis: fructose-1,6-bisphosphatase deficiency; phosphoenolpyruvate carboxylase deficiency; pyruvate carboxylase deficiency.

5. Disorders of fatty acid oxidation and carnitine metabolism: carnitine deficiency; deficiency of enzymes carnitine palmitoyltransferase, acyl-CoA-dehydrogenase, 3-hydroxy-acyl-CoA-dehydrogenase.

6. Disorders of synthesis/utilization of ketone bodies: deficiency of HMG CoA synthase; HMG-CoA lyase deficiency; deficiency of 3-hydroxy acid-CoA-transferase.

7. Metabolic disorders: galactosemia, fructosemia; diseases associated with impaired amino acid synthesis (maple syrup disease; methylmalonic acidemia; propionic acidemia; tyrosinemia); organic acidemias; deficiency of the mitochondrial respiratory chain complex, etc.

In the first month of life, defects in gluconeogenesis and glycogenolysis are rare, as feeding is on demand. Deficiency of acyl-CoA dehydrogenase of medium-chain fatty acids in the neonatal period is usually not manifested. However, it can later cause severe disorders, and its detection should be part of a mass examination of infants.

Features of the clinic of hypoglycemia in infants is the nonspecificity of symptoms that are divided into neuroglycopenic and autonomic. The child manifests itself as a search for food or poor appetite, convulsions, hypotension, palpitations, tremors, sweating. However, the course of hypoglycemia in newborns is often asymptomatic. Hypoglycemia (even asymptomatic) in the newborn period without treatment can lead to brain damage.

Conclusions. Diagnosis of persistent hypoglycemia should include, in addition to assessing the clinical features and results of neonatal screening for hereditary diseases, glucose monitoring, biochemical blood tests for ketone bodies, free fatty acids, ammonium, lactate, bicarbonates, amino acids, acylcarnitines; assessment of blood hormone concentrations (insulin, STG, cortisol, etc.). To detect disorders of amino acid metabolism, organic acids and defects of mitochondrial β-oxidation of fatty acids, it is advisable to conduct tandem mass spectrometry and molecular genetic research. A newborn with persistent hypoglycemia cannot be discharged home without verification of the diagnosis and achievement of normoglycemic values that persist for 72 hours.